Mixtures of chiral monophosphorus compounds used as ligand systems for asymmetric transition metal catalysts

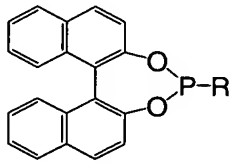
The present invention includes the surprising finding that mixtures of two or more chiral monophosphorus compounds (i.e. compounds having one phosphorus atom) or mixtures consisting of at least one chiral and at least one achiral monophosphorus compound, constitute excellent ligand systems in asymmetric transition metal catalysis. These are in principle novel processes in the field of enantioselective transition metal catalysis in which known or novel chiral monophosphorus compounds are used. In addition, the chiral transition metal catalysts are of a structurally novel type, since two (or more) different monophosphorus compounds are bonded to the metal, of which at least one is a chiral monophosphorus compound. Such metal complexes have never been mentioned in the literature.

Enantioselective transition metal-catalyzed processes have gained significance industrially in the last 20 years, for example the transition metal-catalyzed asymmetric hydrogenation (B. Cornils, W.A. Herrmann, Applied Homogeneous Catalysis with Organometallic Compounds, Wiley-VCH, Weinheim (1996); W.S. Knowles, Angew. Chem., 114, 2096 (2002); R. Noyori, Angew. Chem., 114, 2108 (2002)). The ligands required for this purpose are frequently chiral phosphorus ligands (P ligands), e.g. phosphines, phosphonites, phosphinites, phosphites or phosphoramidites, which are bonded to the transition metals. Typical examples include rhodium, ruthenium or iridium complexes of optically active diphosphines such as BINAP (A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi, R. Noyori, J. Am. Chem. Soc., 102, 7932 (1980)), DuPHOS (M.J. Burk, M.F. Gross, J.P. Martinez, J. Am. Chem. Soc., 117, 9375 (1995)), BICP (G. Zhu, P. Cao,

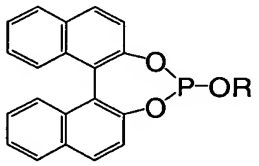
Q. Jiang, X. Zhang, J. Am. Chem. Soc., 119, 1799 (1997) and BPE (M.J. Burk, Y.M. Wang, J.R. Lee, J. Am. Chem. Soc., 118, 5142 (1996)). The development of chiral ligands entails a costly process, consisting of design, and trial and error (W.S. Knowles, Angew. Chem., 114, 2096 (2002)). A supplementary search method is what is known as combinatorial asymmetric catalysis, in which libraries of modularly formed chiral ligands or catalyst systems are prepared and tested, as a result of which the probability of finding a hit is increased (M.T. Reetz, Angew. Chem. 113, 292 (2001); S. Dahmen, S. Bräse, Synthesis, 1431 (2001)). A disadvantage in all of these systems is the relatively high preparative complexity in the preparation of large numbers of ligands, and the often insufficient enantioselectivity which is observed in the catalysis. It is therefore still the aim of industrial and academic research to prepare novel, cheap and particularly high-performance ligands by a very simple route.

While most chiral phosphorus ligands are chelating diphosphorus compounds, such as diphosphines (W.S. Knowles, Angew. Chem., 114, 2096 (2002); R. Noyori, Angew. Chem., 114, 2108 (2002)), diphosphites (for example M.T. Reetz, T. Neugebauer, Angew. Chem., 111, 134 (1999)), diphosphinites (for example R. Selke, J. Organomet. Chem., 370, 249 (1989)) or diphosphonites (for example M.T. Reetz, A. Gosberg, R. Goddard, S.-H. Kyung, Chem. Commun. (Cambridge), 2077 (1998)), which bind and stabilize the particular transition metal as a chelate complex, and thus determine the extent of asymmetric induction in the catalysis, it became known sometime ago that certain chiral monophosphonites (for example M.T. Reetz, T. Sell, Tetrahedron Lett., 41, 6333 (2000); C. Claver, E. Fernandez, A. Gillon, K. Heslop, D.J. Hyett, A. Martorell, A.G. Orpen, P.G. Pringle, Chem. Commun. (Cambridge), 961 (2000)), monophosphites (M.T. Reetz,

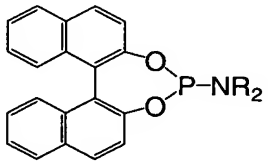
G. Mehler, Angew. Chem., 112, 4047 (2000)) and monophosphoramidites (for example M. van den Berg, A.J. Minnaard, E.P. Schudde, J. van Esch, A.H.M. de Vries, J.G. de Vries, B.L. Feringa, J. Am. Chem. Soc., 122, 11539 (2000)) can likewise be efficient ligands, for example in the rhodium-catalyzed asymmetric hydrogenation of prochiral olefins. Known examples are BINOL-derived representatives, for example the ligands **I**, **II** and **III**. Spectroscopic and mechanistic studies indicate that in each case two monophosphorus ligands are bonded to the metal in the catalysis. Therefore, the metal-ligand ratio is generally 1 : 2. Some chiral monophosphines of the $R^1R^2R^3P$ type may also be good ligands in transition metal catalysis, even though they are generally expensive (for example W.S. Knowles, Angew. Chem., 114, 2096 (2002)).



I a) R = CH_3
b) R = C_2H_5
c) R = c-C_6H_{11}
d) R = $C(CH_3)_3$
e) R = C_6H_5
f) R = Cl



II a) R = CH_3
b) R = C_2H_5
c) R = c-C_6H_{11}
d) R = $C(CH_3)_3$
e) R = C_6H_5
f) R = 2,6-$(CH_3)_2$-C_6H_3
g) R = $CH(CH_3)_2$
h) R = 9-fluorenyl
i) R = $CH_2C_6H_5$



III a) R = CH_3
b) R = $CH(CH_3)_2$

Monophosphorus ligands of the **I - III** type are particularly readily available and can be varied very readily owing to the modular structure (I.V. Komarov, A. Börner, Angew. Chem., 113, 1237 (2001)). Variation of the R radical in **I**, **II** or **III** allows a multitude of chiral ligands to be constructed, as a result of which ligand optimization is possible for a given transition metal-catalyzed reaction (for example hydrogenation of

a prochiral olefin, ketone or imine or hydroformylation of a prochiral olefin). Unfortunately, here too there exist limits of the method, i.e. many substrates are converted with a moderate or poor enantioselectivity, for example in hydrogenations or hydroformylations. Therefore, there is still a need for cheap and effective chiral ligands for industrial application in transition metal catalysis.

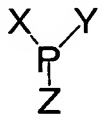
A central constituent of the present invention is the surprising finding that mixtures of two or more monophosphorus compounds of which at least one is chiral lead to higher enantioselectivities in transition metal-catalyzed conversions than the procedure customary hitherto which uses a single, structurally defined monophosphorus ligand. These transition metal catalysts which we have used, in which at least two different monophosphorus ligands (i.e. compounds having one phosphorus atom) are bonded to the metal, at least one monophosphorus ligand being chiral, are novel. These catalysts can be used in a large number of different reaction types for preparing chiral organic compounds from prochiral organic compounds. The optically enriched or pure organic compounds are known to be valuable products or intermediates in industry, for example in the preparation of pharmaceuticals, crop protection agents and fragrances.

Theoretically, the method can always work when at least two monophosphorus ligands (L) are bonded to the metal (M) of the active catalyst ML_x in the transition state of the reaction. Such coordination conditions are known for metals of groups **IIIb, IVb, Vb, VIb, VIIb, VIIIb, Ib** and **IIb** and for the lanthanides and actinides. For example, in the case of a mixture of two such ligands L^a and L^b, three different catalysts present in equilibrium are possible, specifically the traditional homocombinations ML^aL^a and ML^bL^b and the novel

heterocombination ML^aL^b (mixed catalyst). In the literature, many examples of homocombinations can be found, in recent times, for example, the monophosphonites **I**, monophosphites **II** and the monophosphoramidite **III** formed modularly from BINOL, each of which frequently (but not always) enable high enantioselectivities in the Rh-catalyzed olefin hydrogenation. In contrast, heterocombinations ML^aL^b have not yet been described as catalysts. Since rapid ligand exchange is generally to be expected, it should barely be possible to generate ML^aL^b in pure form in solution. However, the mixture of the three catalysts can still lead to a higher enantioselectivity when ML^aL^b acts more rapidly and enantioselectivity than the catalysts ML^aL^a and ML^bL^b used in pure form, and the relative amount of the ligands L^a and L^b might likewise play a role.

In order to illustrate this novel principle in the field of asymmetric transition metal catalysis, the enantioselective Rh-catalyzed olefin hydrogenation of a given substrate with an Rh-phosphonite complex derived from **I** will be described. While traditional use of **I** where $R = R^1$ affords the *ee* value x% for enantioselectivity and traditional use of an analog **I** where $R = R^2$ affords the *ee* value y%, the use of a mixture of both ligands results in a higher enantioselectivity with the *ee* value z%, i.e. $z > x$ and $z > y$. However, this law does not apply to all mixtures. Rather, the increased enantioselectivity is always observed when the correct mixture is selected or the correct selection of the R radicals is made. This is possible rapidly by testing, for example, combinations of different chiral phosphonites, for example of the type I, as mixtures. In the mixture, it is also possible to use more than two different chiral ligands, for example of the type **I**; preference is given to using two.

In addition to mixtures of chiral monophosphonites, of which the BINOL-derived representatives **I** constitute only one of many possibilities, mixtures of other chiral monophosphorus ligands may also be used. Examples are mixtures of chiral monophosphites, for example of the type **II**, or mixtures of monophosphoramidites, for example of the type **III**. However, it is also possible to use chiral phosphines, phosphiranes, phosphinites, phosphorous tris- and bisamides, phosphoric mono- and diamides, and phosphorous diester fluorides, to name just a few. Indeed, any chiral compound having a phosphorus atom is useful. In practice, there is a wealth of possible phosphorus ligands whose central skeleton is shown by the following formula **IV**.



IV

In the formula, the X, Y and Z atoms may each independently be from the group of carbon (C), nitrogen (N), oxygen (O), sulfur (S) or halogen (F, Cl, Br, I). Further atoms or groups of atoms are bonded each independently to the X, Y and Z atoms according to their number of free valences, as, for example, in the examples **I**, **II** and **III** already mentioned. X, Y and Z may also be connected together by the bonded atoms or groups of atoms, and X-P-Y may also be part of an aromatic system, in which case X is then bonded to P by a double bond and there is no substituent Z.

The following combinations of substituents on **IV** are mentioned by way of example:

a) X = Y = Z = C

b) X = Y = C; Z = N

c) X = Y = C; Z = O

d) X = Y = C; Z = S

e) X = Y = C; Z = halogen (F, Cl, Br or I)

f) X = C; Y = Z = N

g) X = C; Y = Z = O

h) X = C; Y = Z = S

i) X = C; Y = N; Z = O

j) X = Y = Z = N

k) X = Y = N; Z = O

l) X = Y = N; Z = S

m) X = Y = N; Z = halogen (F, Cl, Br or I)

n) X = N; Y = Z = O

o) X = N; Y = Z = S

p) X = N; Y = O; Z = halogen (F, Cl, Br or I)

q) X = Y = Z = O

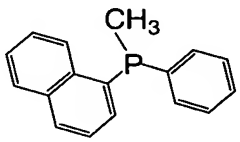
r) X = Y = O; Z = alogen (F, Cl, Br or I)

s) X = Y = Z = S

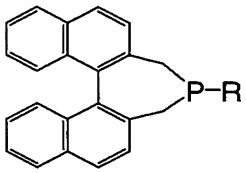
Further examples of representatives are analogs of **I**, **II** and **III** in which the axially chiral building block BINOL is replaced by derivatives, substituted biphenols or by other chiral diols. Specific representatives are, for example, 5,5'-dichloro-6,6'-dimethoxy-2,2'-biphenol, hydrobenzoin, TADDOL and diols derived from carbohydrates. However, these are just a few possible examples whose mention in no way restricts the extent of the possibilities. Since the ligands **IV** are formed modularly, this means that the particular building blocks are, for example, chiral alcohols, chiral diols, chiral amines, chiral diamines or chiral amino alcohols, to name just the most important possibilities. In the examples which follow, the absolute chirality is not illustrated. However, it is

self-evident that any ligand can be used in any possible configuration. The ligands are used in an enantiomerically pure or enriched form. Preference is given to utilizing enantiomerically pure ligands.

Typical examples of chiral ligands **IVa** are **V** and **VI**, which have central and axial chirality respectively:

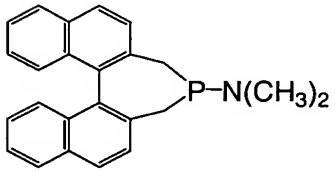


V

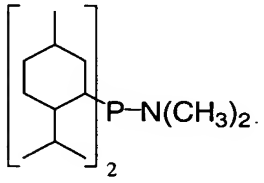


VI (R = alkyl, aryl, alkoxy, amino, halogen)

Typical examples of chiral ligands **IVb** are **VII** and **VIII**:

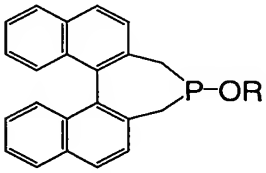


VII

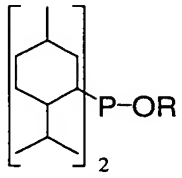


VIII

Typical examples of chiral ligands **IVc** are **IX** and **X**:



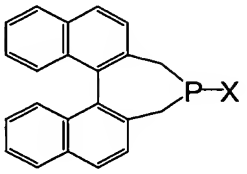
IX (R = alkyl, aryl)



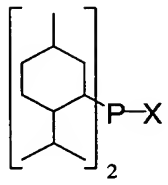
X (R = alkyl, aryl)

Typical examples of chiral ligands **IVd** are the thio analogs of **IX** and **X**.

Typical examples of chiral ligands **IVe** are **XI** and **XII**:

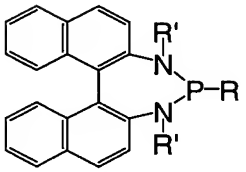


XI (X = F, Cl, Br or I)

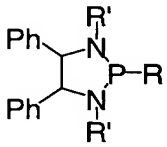


XII (X = F, Cl, Br or I)

Typical examples of chiral ligands **IVf** are **XIII** and **XIV**:



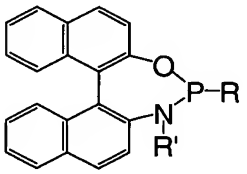
XIII (R = alkyl, aryl;
R' = alkyl, aryl, sulfonyl)



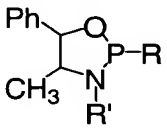
XIV (R = alkyl, aryl;
R' = alkyl, aryl, sulfonyl)

Typical examples of chiral ligands **IVg** and **IVh** are compounds **I** and the thio analogs.

Typical examples of chiral ligands **IVi** are **XV** and **XVI**:

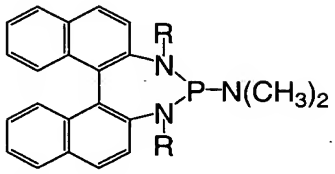


XV (R = alkyl, aryl;
R' = alkyl, aryl, sulfonyl)

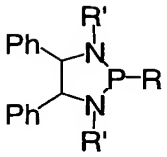


XVI (R = alkyl, aryl;
R' = alkyl, aryl, sulfonyl)

Typical examples of chiral ligands **IVj** are **XVII** and **XVIII**:

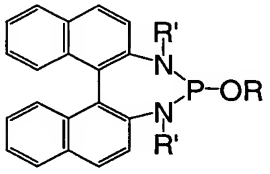


XVII (R = alkyl, aryl, sulfonyl)

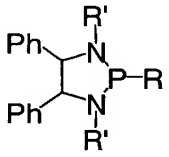


XVIII (R = alkyl, aryl;
R' = alkyl, aryl, sulfonyl)

Typical examples of chiral ligands **IVk** are **XIX** and **XX**:



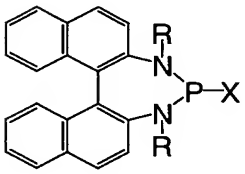
XIX (R = alkyl, aryl;
R' = alkyl, aryl, sulfonyl)



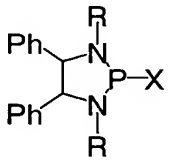
XX (R = alkyl, aryl;
R' = alkyl, aryl, sulfonyl)

Typical examples of chiral ligands **IVl** are the thio analogs of **XIX** and **XX**.

Typical examples of chiral ligands **IVm** are **XXI** and **XXII**:



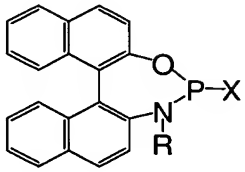
XXI (X = F, Cl, Br or I;
R = alkyl, aryl, sulfonyl)



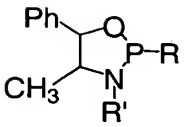
XXII (X = F, Cl, Br or I;
R = alkyl, aryl, sulfonyl)

Typical examples of chiral ligands **IVn** and **IVo** are **III** and the thio analogs of **III** respectively.

Typical examples of chiral ligands **IVp** are **XXIII** and **XXIV**:



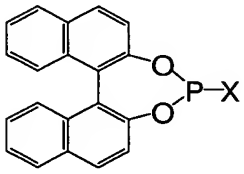
XXIII (X = F, Cl, Br or I; R = alkyl, aryl, sulfonyl)



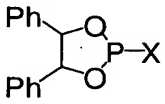
XXIV (X = F, Cl, Br or I; R = alkyl, aryl, sulfonyl)

Typical examples of chiral ligands **IVq** and **IVs** are **II** and the thio analogs of **II**, respectively.

Typical examples of chiral ligands **IVr** are **XXV** and **XXVI**:



XXV (X = F, Cl, Br or I)



XXVI (X = F, Cl, Br or I)

The underlying principle of the invention does not only apply when the chiral phosphorus ligands belong to the same substance class. An increase in the enantioselectivity is observed even when the mixture is of two (or more) chiral monophosphorus ligands which belong to different classes of phosphorus compounds **IV**.

A second variant of the invention likewise includes the mixture of two different phosphorus ligands, one of which (as described above) includes chirality, but the other is achiral. The use of a correct combination of a chiral ligand **IV** and an achiral analog **IV** leads in transition metal catalysis even in such cases surprisingly to a higher enantioselectivity than in the case of use of the relevant chiral ligand alone. In

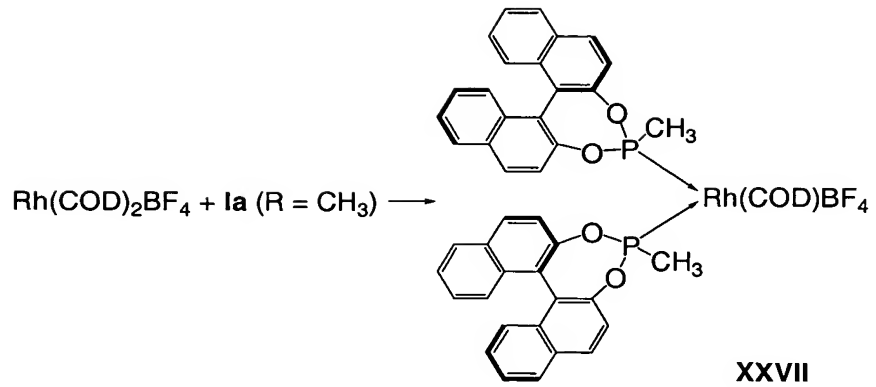
some cases, such a combination can even be used to reverse the direction of enantioselectivity.

The achiral phosphorus ligands can likewise be described correspondingly by the general formula **IV**. They are thus, for example, achiral phosphines, phosphinites, phosphonites, phosphorous tris- and bisamides, phosphoric mono- and diamides, to name just a few. Representatives where X = Y = Z = halogen, i.e. PF_3, PCl_3, PBr_3 or PI_3, and also thiophosphites $P(SR)_3$, phosphine oxides, phosphine sulfides, iminophosphoranes, phosphiranes and phosphinines are also useful.

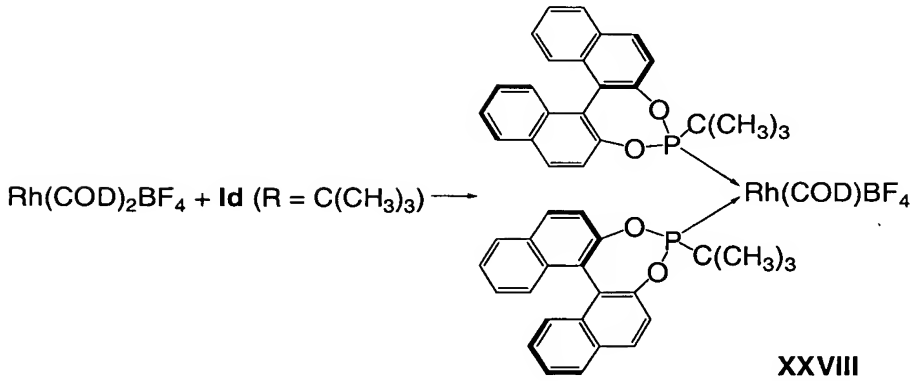
As far as the preparation of the catalysts or precatalysts is concerned, the procedure known in the literature which is used typically to prepare traditional homocombinations $M(L^a)_n$ is useful. This means that the particular ligands mixture is combined with a suitable transition metal complex. The transition metal complexes may be common salts such as MX_n (X = F, Cl, Br, I, BF_4, ClO_4, RCO_2, RSO_3 acac), for example $[Rh(OAc)_2]_2$, $Rh(acac)_3$, $Cu(CF_3SO_3)_2$, $CuBF_4$, $Ag(CF_3SO_3)$, Au(CO)Cl, $In(CF_3SO_3)_3$, $Fe(ClO_4)_3$, $NiCl_2(COD)$ (COD = 1,5-cyclooctadiene), $Pd(OAc)_2$, $[C_3H_5PdCl]_2$, $PdCl_2(CH_3CN)_2$ or $La(CF_3SO_3)_3$, to name just a few. However, they may also be metal complexes which bear ligands including olefins, dienes, pyridine, CO or NO (to name just a few). The latter are displaced fully or partly by the reaction with the phosphorus ligands. Cationic metal complexes may likewise be used. Those skilled in the art know a multitude of possibilities (G. Wilkinson, Comprehensive Coordination Chemistry, Pergamon Press, Oxford (1987); B. Cornils, W.A. Herrmann, Applied Homogeneous Catalysis with Organometallic Compounds, VCH, Weinheim (1996)). Common examples are $Rh(COD)_2BF_4$, $[(cymene)RuCl_2]_2$, $(pyridine)_2Ir(COD)BF_4$, $Ni(COD)_2$, $(TMEDA)Pd(CH_3)_2$

(TMEDA = *N, N, N', N'*-tetramethylenediamine), $Pt(COD)_2$, $PtCl_2(COD)$ or $[RuCl_2(CO)_3]_2$, to name just a few. The metals include those of groups **IIIb**, **IVb**, **Vb**, **VIb**, **VIIb**, **VIII**, **Ib** and **IIb** of the periodic table, and lanthanides and actinides.

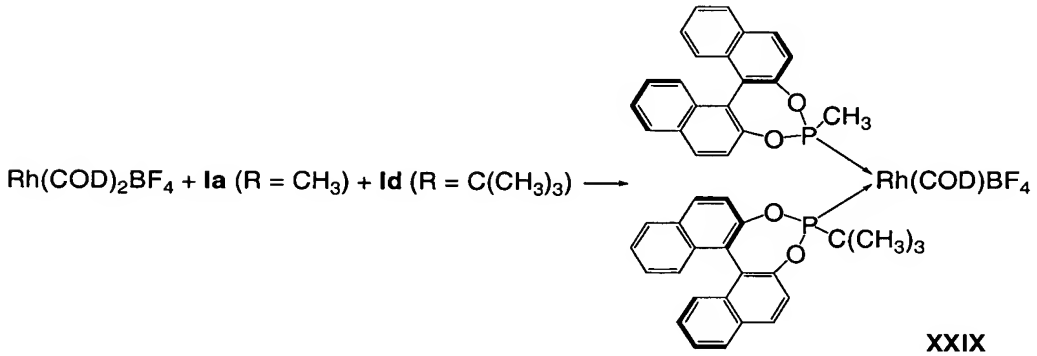
For illustration and for verification that the catalysts are structurally novel, the reactions of $Rh(COD)_2BF_4$ with the pure (R)-configured phosphonites **I** ($R = CH_3$) and **I** ($R = C(CH_3)_3$) to form the traditional Rh complexes **XXVII** and **XXVIII** and the reaction with a 1 : 1 mixture of both ligands to form the "mixed" complex **XXIX** (as well as the complexes **XXVII** and **XXVIII**) will be mentioned. The ^1H, ^{13}C and ^{31}P-NMR spectra of the complex **XXIX** are characteristic of a "mixed" compound, i.e. they differ from the spectra of the conventional complexes **XXVII** and **XXVIII**. When the mixture of the complexes **XXVII**, **XXVIII** and **XXIX** is isolated, it is possible by mass spectrometry (ESI-MS) to unambiguously detect all three complexes, **XXIX** being the main component. As far as practical application is concerned, the "mixed complex" **XXIX** does not necessarily have to be separated from the pure complexes **XXVII** and **XXVIII**, since it is found on the basis of kinetic investigations that the mixture of the three catalysts is more active than the particular homocombinations **XXVII** and **XXVIII**. Analogous NMR and ESI-MS analyses of other "mixed" metal catalysts (heterocombinations) likewise prove the unique structure of these complexes and demonstrate that it is a new substance class.



XXVII



XXVIII



XXIX

A crucial factor for the invention is the unexpected finding that the overall catalysis profile of the traditional catalysts, for example **XXVII** and **XXVIII**, differs greatly from that of the "mixed" complex, for example **XXIX**. It is found that, for example, in an olefin hydrogenation, the inventive catalyst **XXIX** affords a distinctly higher enantioselectivity than is achieved when the traditional catalysts **XXVII** and **XXVIII** are used. At the same time, a higher rate of

reaction is observed. As far as the practical side is concerned, a separation and purification of the "mixed" catalyst **XXIX** is therefore not necessarily required, i.e. the mixture of **XXIX** and **XXVII/XXVIII** can be used, since the high activity of **XXIX** determines the catalytic result. A further typical example relates to the reaction of $Rh(COD)_2BF_4$ with a 1:1 mixture of **Ic** and **IIa** which leads to the mixture of $Rh(\mathbf{Ic})_2(COD)BF_4$, $Rh(\mathbf{IIa})_2(COD)BF_4$ and $Rh(\mathbf{Ic})(\mathbf{IIa})(COD)BF_4$. Here too, investigations show that the heterocombination has different spectroscopic properties than the traditional homocombinations.

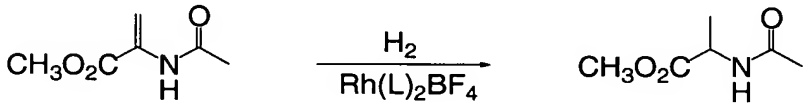
The inventive "mixed catalysts" based on heterocombinations of different monophosphorus compounds may contain a plurality of chiral or achiral phosphorus ligands, preferably two different phosphorus ligands. The ratio of the phosphorus ligands relative to one another in the metal complex may be varied as desired. When there are, for example, two different ligands A and B, the relative ratio A : B may preferably be varied between 1 : 4 and 4 : 1; particular preference is given to selecting an A : B ratio of approx. 1 : 1. The ratio of metal to substrate moves within the customary range, i.e. between 1 : 5 and 1 : 1 000 000.

The searching of libraries of mixtures of two chiral monophosphorus ligands or of mixtures of one chiral and one achiral phosphorus ligand provides the simple means of finding the best mixed catalyst (heterocombination) for a given transition metal-catalyzed conversion. This procedure is simple and can be performed rapidly with modern instruments which are customary in combinatorial catalysis. These include parallelized reactors and pipetting robots (M.T. Reetz, Angew. Chem., 113, 292 (2001)). However, a sequential procedure is also possible, i.e. one mixture can be tested after another. The inventive use of two (or more) chiral

monophosphorus ligands or mixtures of chiral and achiral monophosphorus ligands applies to all transition metal-catalyzed reactions (E.N. Jacobsen, A. Pfaltz, H. Yamamoto, Comprehensive Asymmetric Catalysis, Vol. I-III, Springer, Berlin (1999)), in particular to asymmetric hydrogenations, hydroformylations, hydroborations, hydrosilylations, hydrovinylations, hydroaminations, epoxidations, hydroxylations, aminohydroxylations, substitutions (for example allyl substitutions), Heck, Stille, Suzuki and Negishi couplings, Michael additions, aldol additions, Diels-Alder reactions, cyclopropanations, CH insertion reactions and 1,3-dipolar cycloadditions.

Examples

Example 1: Rh-catalyzed hydrogenation of methyl *N*-acylacrylate using ligands of the **I, II** and **III** type



A baked-out 50 ml Schlenk vessel was initially charged under an argon atmosphere with a mixture of 0.6 ml of a 1.7 mM solution of the first ligand and 0.6 ml of a 1.7 mM solution of the second ligand in abs. dichloromethane. This solution was admixed with 0.5 ml of a 2.0 mM solution of $[Rh(COD)_2]BF_4$ in dichloromethane and stirred at room temperature for 5 minutes. Subsequently, 9 ml of a 0.112 M solution of the substrate in dichloromethane were added. The vessel was three times evacuated until the solvent was boiling gently and aerated with hydrogen. At hydrogen pressure 1.3 bar, the mixture was stirred for the duration of the reaction. The conversion was determined by gas chromatography after dilution of the reaction solution.

For the determination of the enantiomeric excess, approx. 1.5 ml of the reaction solution were filtered adsorptively through a little silica gel and analyzed by gas chromatography or by means of HPLC. The experiments were carried out with 20 vessels in parallel.

For comparison, the pure ligands were tested under otherwise identical conditions in the Rh-catalyzed hydrogenation. The results are compiled in table 1. According to these, there are actually several mixed catalysts (heterocombinations) that are distinctly more enantioselective (for example entries 16, 17, 40, 42, 44 and 45) than the analogs formed from traditional pure ligands (entries 1 - 14).

Table 1. Rh-catalyzed hydrogenation of **IVa**[a]

Entry	Ligands	*ee* [%] (config.)
	Homocombinations	
1	(*R*)**Ia**/(*R*)**Ia**	91.8 (*S*)
2	(*R*)**Ib**/(*R*)**Ib**	94.4 (*S*)
3	(*R*)**Ic**/(*R*)**Ic**	92.0 (*S*)
4	(*R*)**Id**/(*R*)**Id**	93.3 (*S*)
5	(*R*)**Ie**/(*R*)**Ie**	72.8 (*S*)
6[b]	(*R*)**If**/(*R*)**If**	7.4 (*S*)
7	(*S*)**IIa**/(*S*)**IIa**	76.6 (*R*)
8	(*S*)**IIb**/(*S*)**IIb**	83.6 (*R*)
9	(*R*)**IIc**/(*R*)**IIc**	94.6 (*S*)
10	(*S*)**IId**/(*S*)**IId**	95.4 (*R*)
11[c]	(*S*)**IIe**/(*S*)**IIe**	78.6 (*R*)
12[d]	(*S*)**IIf**/(*S*)**IIf**	32.4 (*R*)
13	(*S*)**IIg**/(*S*)**IIg**	94.4 (*R*)
14	(*S*)**IIh**/(*S*)**IIh**	92.4 (*R*)
	Heterocombinations	
15	(*R*)**Ia**/(*R*)**Ib**	92.6 (*S*)
16	(*R*)**Ia**/(*R*)**Ic**	97.9 (*S*)
17	(*R*)**Ia**/(*R*)**Id**	97.8 (*S*)
18	(*R*)**Ic**/(*R*)**Id**	94.1 (*S*)

Entry	Ligands	*ee* [%] (config.)
19	(*R*)**Id**/(*R*)**Ie**	75.8 (*S*)
20	(*R*)**Id**/(*R*)**If**	racemic
21	(*R*)**IIa**/(*R*)**IIb**	80.0 (*S*)
22	(*R*)**IIa**/(*R*)**IIc**	76.6 (*S*)
23	(*R*)**IIa**/(*R*)**IId**	89.0 (*S*)
24	(*R*)**IIa**/(*R*)**IIe**	77.4 (*S*)
25	(*R*)**IIa**/(*R*)**IIf**	84.6 (*S*)
26	(*R*)**IIa**/(*R*)**IIg**	87.2 (*S*)
27	(*R*)**IIb**/(*R*)**IIc**	79.0 (*S*)
28	(*R*)**IIb**/(*R*)**IId**	91.2 (*S*)
29	(*R*)**IIb**/(*R*)**IIe**	80.8 (*S*)
30	(*R*)**IIb**/(*R*)**IIg**	90.0 (*S*)
31	(*R*)**IId**/(*R*)**IIc**	94.2 (*S*)
32	(*R*)**IId**/(*R*)**IIe**	92.2 (*S*)
33	(*R*)**IIe**/(*R*)**IIc**	73.6 (*S*)
34	(*R*)**IIg**/(*R*)**IIc**	94.6 (*S*)
35	(*R*)**IIg**/(*R*)**IId**	94.8 (*S*)
36	(*R*)**IIg**/(*R*)**IIe**	91.2 (*S*)
37	(*R*)**Ia**/(*R*)**IIa**	81.9 (*S*)
38	(*R*)**Ia**/(*R*)**IIc**	94.4 (*S*)
39	(*R*)**Ia**/(*R*)**IId**	93.0 (*S*)
40	(*R*)**Ic**/(*R*)**IIa**	96.4 (*S*)
41	(*R*)**Ic**/(*R*)**IId**	91.8 (*S*)
42	(*R*)**Id**/(*R*)**IIa**	98.0 (*S*)
43	(*R*)**Id**/(*R*)**IIc**	94.6 (*S*)
44	(*R*)**Id**/(*R*)**IIh**	97.2 (*S*)
45	(*R*)**Ic**/(*R*)**IIh**	95.6 (*S*)

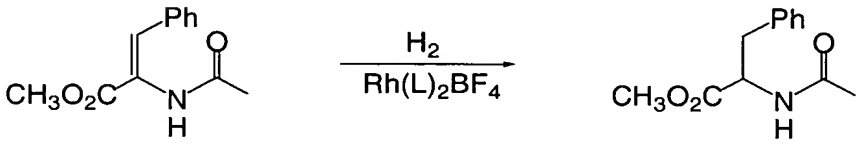
[a] Rh/substrate ratio 1 : 1000; Rh/P ratio 1 : 2; solvent: CH_2Cl_2; p(H_2): 1.3 bar; T: 20°C; reaction time: 20 h; conversion: 100%.

[b] Conversion: 1%.

[c] Conversion: 93%.

[d] Conversion: 62%.

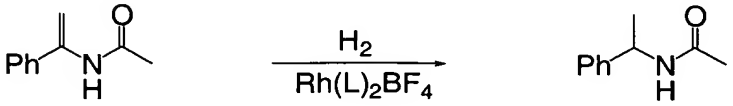
Example 2: Rh-catalyzed hydrogenation of methyl phenyl-*N*-acylacrylate using ligands of the **I** type



A baked-out 50 ml Schlenk vessel was initially charged under an argon atmosphere with a mixture of 0.6 ml of a 1.7 mM solution of the first ligand and 0.6 ml of a 1.7 mM solution of the second ligand in abs. dichloromethane. This solution was admixed with 0.5 ml of a 2.0 mM solution of $[Rh(COD)_2]BF_4$ in dichloromethane and stirred at room temperature for 5 minutes. Subsequently, 9 ml of a 0.112 M solution of the substrate in dichloromethane were added. The vessel was three times evacuated until the solvent was boiling gently and aerated with hydrogen. At hydrogen pressure 1.3 bar, the mixture was stirred for the duration of the reaction. The conversion was determined by gas chromatography after dilution of the reaction solution. For the determination of the enantiomeric excess, approx. 1.5 ml of the reaction solution were filtered adsorptively through a little silica gel and analyzed by gas chromatography or by means of HPLC. The experiments were carried out with 20 vessels in parallel.

The measured enantioselectivities at 100% conversion are as follows: (*R*)**Ia**/(*R*)**Ic**: *ee* = 96.7% (*S*); (*R*)**Ia**/(*R*)**Id**: *ee* = 99.2% (*S*); (*R*)**Ib**/(*R*)**Id**: *ee* = 94.6% (*S*) compared to (*R*)**Ia**/(*R*)**Ia**: *ee* = 89.9% (*S*); (*R*)**Ib**/(*R*)**Ib**: *ee* = 89.2% (*S*); (*R*)**Id**/(*R*)**Id**: *ee* = 69.1% (*S*).

Example 3: Rh-catalyzed hydrogenation of 1-*N*-acylaminostyrene using ligands of the **I and II** type



Analogously to the method in example 1, a mixture of 0.5 ml of a 2 mM solution of $Rh(COD)_2BF_4$ in dry CH_2Cl_2, 0.25 ml of a 4 mM solution of a phosphonite **I** and 0.25 ml of a 4 mM solution of a second phosphonite **I** in CH_2Cl_2 were prepared. This led to a change in the color from orange to yellow. After 1-*N*-acylaminostyrene (0.5 mM) in 1 ml of CH_2Cl_2 had been added, the reaction solution was stirred at 30°C and 1.5 bar of H_2 pressure for 22 hours. The GC analysis gives the conversion and the *ee* value.

Rh-catalyzed hydrogenation of 1-N-acetamidostyrene

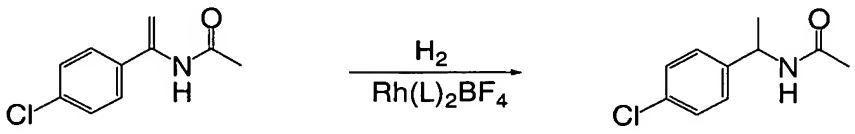
Entry	Ligands	ee (%) configuration
	Homocombinations	
1	**(*R*)Ia/(*R*)Ia**	75.6 (*S*)
2[b]	**(*R*)Id/(*R*)Id**	83.0 (*S*)
3	**(*R*)IIa/(*R*)IIa**	76.0 (*S*)
4	**(*R*)IIc/(*R*)IIc**	84.8 (*S*)
5	**(*R*)IIe/(*R*)IIe**	85.4 (*S*)
6	**(*R*)IIi/(*R*)IIi**	91.4 (*S*)
	Heterocombinations	
7[c]	**(*R*)Ia/(*R*)Id**	96.1 (*S*)
8	**(*R*)IIa/(*R*)Id**	95.0 (*S*)
9	**(*R*)IIe/(*R*)IIc**	88.6 (*S*)
10	**(*R*)IIi/(*R*)Id**	97.4 (*S*)

[a] Rh/substrate ratio 1:500, rest as table 1

[b] Conversion: 13%

[c] Conversion: > 95%

Example 4: Rh-catalyzed hydrogenation of 1-*N*-acylamino-1-*p*-chlorophenylethylene



The hydrogenations are effected analogously to the method in example 3. The measured enantioselectivities at > 95% conversion are as follows: (*R*)**Ia**/(*R*)**Id**: *ee* = 95.0% (*S*) compared to (*R*)**Ia**/(*R*)**Ia**: *ee* = 73.0% (*S*) and (*R*)**Id**/(*R*)**Id**: *ee* = 16.2% (*S*), conversion 79%.

Example 5: Variation of the ratio of the two phosphorus ligands **Ia** and **Id** in the Rh-catalyzed hydrogenation of 1-*N*-acylaminostyrene

The hydrogenations were carried out as in example 3, but with variation of the relative ratio of **Ia** and **Id**. The Rh : P ratio was kept constant at 1 : 2 and the Rh : substrate ratio at 1 : 500. The enantioselectivities determined by means of GC at conversions of > 95% are compiled in table 2.

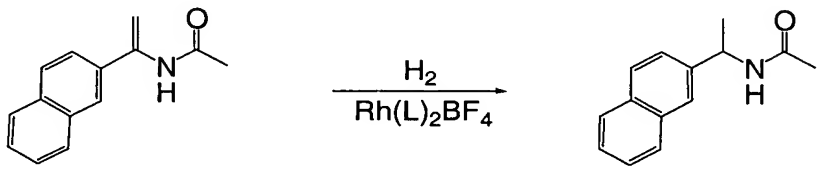
Table 2.
Influence of the **Ia** : **Id** ratio on the enantioselectivity of the hydrogenation of **VIa**[a]

Entry	Ligands (*R*)**Ia**/(*R*)**Id**	*ee* [%] (config.)
1[b]	1 : 5	95.4 (*S*)
2	1 : 3	97.4 (*S*)
3	1 : 2	97.2 (*S*)
4	1 : 1	96.4 (*S*)
5	2 : 1	88.8 (*S*)
6	3 : 1	85.0 (*S*)
7	5 : 1	81.2 (*S*)

[a] In all cases, the Rh/((*R*)**Ia**/(*R*)**Id**) ratio was 1 : 2 and the Rh/substrate ratio 1 : 500. Solvent: CH_2Cl_2; p(H_2): 1.5 bar; T: 20°C; reaction time: 1 h; conversion: 100%.

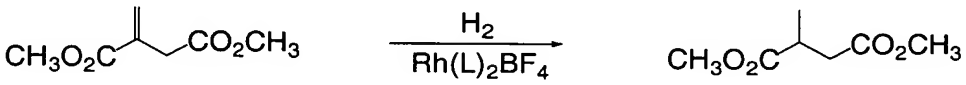
[b] Conversion: 95%.

Example 6: Rh-catalyzed hydrogenation of 1-*N*-acylamino-1-naphthylethylene using ligands of the **I** type



The hydrogenations were effected analogously to the method in example 3. The measured enantioselectivities at > 95% conversion are as follows: (*R*)**Ia**/(*R*)**Id**: *ee* = 97.0% (*S*) compared to (*R*)**Ia**/(*R*)**Ia**: *ee* = 78.2% (*S*) and (*R*)**Id**/(*R*)**Id**: *ee* = < 3% (*S*), conversion 35%.

Example 7: Rh-catalyzed hydrogenation of dimethyl itaconate using ligands of the **I** type



The hydrogenation was effected analogously to the method in example 1. The enantioselectivities determined by means of GC at quantitative conversion are compiled in table 3.

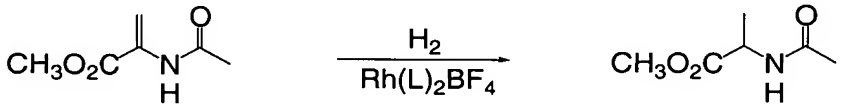
Table 3. Rh-catalyzed hydrogenation of **VIII**[a]

Entry	Ligands	ee [%] (config.)
	Homocombinations	
1	(*R*)**Ia**/(*R*)**Ia**	90.2 (*R*)
2	(*R*)**Ib**/(*R*)**Ib**	71.4 (*R*)
3	(*R*)**Ic**/(*R*)**Ic**	21.9 (*R*)
4	(*R*)**Id**/(*R*)**Id**	57.3 (*R*)
5	(*R*)**Ie**/(*R*)**Ie**	28.8 (*R*)
	Heterocombinations	
6	(*R*)**Ia**/(*R*)**Ib**	82.4 (*R*)
7	(*R*)**Ia**/(*R*)**Ic**	88.6 (*R*)
8	(*R*)**Ia**/(*R*)**Id**	96.4 (*R*)
9	(*R*)**Ib**/(*R*)**Id**	92.2 (*R*)
10	(*R*)**Ic**/(*R*)**Id**	69.1 (*R*)
11	(*R*)**Ic**/(*R*)**Ie**	50.0 (*R*)
12	(*R*)**Id**/(*R*)**Ie**	57.4 (*R*)

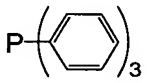
[a] In all cases, the Rh/P ratio was 1 : 2 and the Rh/substrate ratio 1 : 1000. Solvent: CH_2Cl_2; $p(H_2)$: 1.3 bar; T: 20°C, reaction time: 20 h; conversion: 100%.

The quantitative hydrogenation may also be carried out with reduction of the Rh/substrate ratio under otherwise identical conditions. At Rh : substrate = 1 : 6000, the *ee* value is 95.8% (*R*); at 1 : 10 000, the *ee* value is 95.4% (*R*); at 1 : 20 000, the *ee* value is 94.6% (*R*).

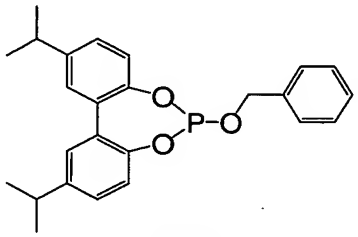
Example 8: Rh-catalyzed hydrogenation of methyl *N*-acylaminoacrylate using chiral phosphonites **I**, phosphites **II**, phosphoramidites **III** and achiral monophosphorus ligands



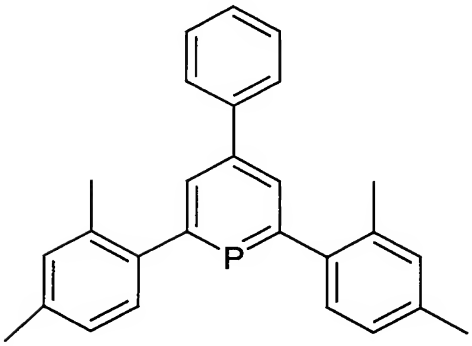
The conditions of the hydrogenations were as selected in example 1, except that a chiral phosphorus ligand (compound **I** or **II**) and an achiral phosphorus ligand (compound **XXX** or **XXXI**) were used in a ratio of 1 : 1.



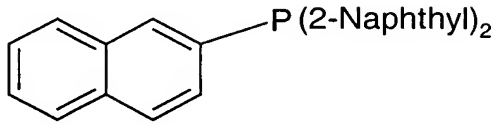
XXX



XXXI



XXXII



XXXIII

The results of the hydrogenation with reversal of the enantioselectivity at quantitative conversion are as follows:

Entry	Ligands	ee (%) configuration
1	**(*R*)Ia/XXX**	19.6 (*R*)
2	**(*R*)IIa/XXX**	10.0 (*R*)
3	**(*R*)IId/XXX**	45.4 (*R*)
4	**(*R*)Ia/XXXII**	58.6 (*R*)
5	**(*R*)Id/XXXII**	52.6 (*R*)
6	**(*R*)IId/XXXIII**	34.8 (*R*)

Rh/substrate ratio 1 : 1000; Rh/P ratio 1 : 2; solvent:

CH_2Cl_2; p(H_2): 1.3 bar; T: 20°C; reaction time: 20 h; conversion: 100%.

Example 9: Preparation and characterization of the catalyst system Rh[**Ia**][**Id**][COD]BF_4 + Rh[**Ia**]$_2$[COD]BF_4 + Rh[**Id**]$_2$[COD]BF_4

The mixture of (*R*)**Ia** (13.2 mg; 0.04 mmol) and (*R*)**Id** (14.9 mg; 0.04 mmol) in CD_2Cl_2 (1 ml) was treated with Rh[COD]$_2BF_4$ (16.2 mg; 0.04 mmol) in CD_2Cl_2 (1 ml). The ^1H, ^{13}C and ^{31}P NMR spectra show the presence of the two homocombinations Rh[(*R*)**Ia**]$_2$[COD]BF_4 (**XXVII**) and Rh[(*R*)**Id**]$_2$[COD]BF_4 (**XXVIII**) and the heterocombination Rh[(*R*)**Ia**][(*R*)**Id**]BF_4 (**XXIX**) in a ratio of about 20 : 20 : 60. The characteristic peaks and distributions in the ^{31}P spectrum are as follows:

^{31}P NMR (121.5 MHz, 223 K, CD_2Cl_2, rel. ext. 85% H_3PO_4):

	δ_P (Ia)	δ_P (Id)	J_{RhP}, Hz	J_{PP}, Hz	%
Rh[(*R*)**Ia**]$_2$[COD]BF_4	189.8		206		18
Rh[(*R*)**Id**]$_2$[COD]BF_4		204.8	207		23
Rh[(*R*)**Ia**][(*R*)**Id**][COD]BF_4 (1st isomer)	187.0	208.3	208, 210	38	15
Rh[(*R*)**Ia**][(*R*)**Id**][COD]BF_4 (2nd isomer)	202.4, 201.8		201, 212	40	44

Example 10: Preparation, isolation and characterization of the catalyst system Rh[**Ia**][**Id**][COD]BF_4 + Rh[**Ia**]$_2$[COD]BF_4 + Rh[**Id**]$_2$[COD]BF_4 by means of ESI-MS

A mixture of (*R*)**Ia** (32.6 mg; 0.1 mmol) and (*R*)**Id** (36.9 mg; 0.1 mmol) in CH_2Cl_2 (20 ml) was admixed at -78°C with Rh[COD]$_2BF_4$ (40.7 mg; 0.1 mmol) in CH_2Cl_2 (5 ml). After warming to room temperature, the solvent was concentrated to 5 ml and a yellow solid was precipitated with 15 ml of pentane. This was washed three times with pentane and dried under reduced pressure. In the ESI-MS spectrum, fragments of the

complexes described in example 9 can be detected, the complex **XXIX** of the heterocombination constituting the main component. The ^{31}P NMR spectrum in CD_2Cl_2 shows the same signals as have already been described and assigned in example 9.

$Rh[(R)\mathbf{Ia}]_2[COD]BF_4$ (**XXVII**):

MS(ESI/pos. in CH_2Cl_2): m/z = 763 $[M^+-BF_4-COD]$.

$Rh[(R)\mathbf{Id}]_2[COD]BF_4$ (**XXVIII**):

MS(ESI/pos. in CH_2Cl_2): m/z = 847 $[M^+-BF_4-COD]$.

$Rh[(R)\mathbf{Ia}][(R)\mathbf{Id}][COD]BF_4$ (**XXIX**):

MS(ESI/pos. in CH_2Cl_2): m/z = 805 $[M^+-BF_4-COD]$.

Example 11: Analysis of a mixture of $Rh[\mathbf{Ia}]_2[COD]BF_4$ and $Rh[\mathbf{Id}]_2[COD]BF_4$

A solution of $Rh[\mathbf{Ia}]_2[COD]BF_4$ (3.3 mg; 0.0034 mmol; 0.5 ml of CD_2Cl_2) and a solution of $Rh[\mathbf{Id}]_2[COD]BF_4$ (3.5 mg; 0.0034 mmol; 0.5 ml of CD_2Cl_2) were mixed. The mixture was analyzed by ^{31}P NMR spectroscopy. With reference to the signals (analogously to example 9), it is found that the same components $Rh[(R)\mathbf{Ia}]_2[COD]BF_4$ (**XXVII**), $Rh[(R)\mathbf{Id}]_2[COD]BF_4$ (**XXVIII**) and $Rh[(R)\mathbf{Ia}][(R)\mathbf{Id}]BF_4$ (**XXIX**) are present as in example 9.

Example 12: Preparation, isolation and characterization of the catalyst system $Rh[\mathbf{Ia}][\mathbf{Ic}][COD]BF_4$ + $Rh[\mathbf{Ia}]_2[COD]BF_4$ + $Rh[\mathbf{Ic}]_2[COD]BF_4$ by means of ESI-MS

A mixture of $(R)\mathbf{Ia}$ (29.4 mg; 0.09 mmol) and $(R)\mathbf{Ic}$ (35.5 mg; 0.09 mmol) in CH_2Cl_2 (20 ml) was admixed at - 78°C with $Rh[COD]_2BF_4$ (36.5 mg; 0.09 mmol) in CH_2Cl_2 (5 ml). After warming to room temperature, the solvent was concentrated to 5 ml and a yellow solid was precipitated with 15 ml of pentane. This was washed

three times with pentane and dried under reduced pressure. In the ESI-MS spectrum, the following fragments can be detected:

$Rh[(R)\mathbf{Ia}]_2[COD]BF_4$:

MS(ESI/pos. in CH_2Cl_2): m/z = 763 $[M^+-BF_4-COD]$.

$Rh[(R)\mathbf{Ic}]_2[COD]BF_4$:

MS(ESI/pos. in CH_2Cl_2): m/z = 897 $[M^+-BF_4-COD-2H]$.

$Rh[(R)\mathbf{Ia}][(R)\mathbf{Ic}][COD]BF_4$:

MS(ESI/pos. in CH_2Cl_2): m/z = 831 $[M^+-BF_4-COD]$.

Example 13: Preparation, isolation and characterization of the catalyst system $Rh[\mathbf{IIa}][\mathbf{Ic}][COD]BF_4$ + $Rh[\mathbf{IIa}]_2[COD]BF_4$ + $Rh[\mathbf{Ic}]_2[COD]BF_4$ by means of ESI-MS

A mixture of $(R)\mathbf{IIa}$ (44.6 mg; 0.13 mmol) and $(R)\mathbf{Ic}$ (51.8 mg; 0.13 mmol) in CH_2Cl_2 (20 ml) was admixed at -78°C with $Rh[COD]_2BF_4$ (52.8 mg; 0.13 mmol) in CH_2Cl_2 (5 ml). After warming to room temperature, the solvent was concentrated to 5 ml and a yellow solid was precipitated with 15 ml of pentane. This was washed three times with pentane and dried under reduced pressure. In the ESI-MS spectrum, the following fragments can be detected:

$Rh[(R)\mathbf{IIa}]_2[COD]BF_4$:

MS(ESI/pos. in CH_2Cl_2): m/z = 795 $[M^+-BF_4-COD]$.

$Rh[(R)\mathbf{Ic}]_2[COD]BF_4$:

MS(ESI/pos. in CH_2Cl_2): m/z = 897 $[M^+-BF_4-COD-2H]$.

$Rh[(R)\mathbf{IIa}][(R)\mathbf{Ic}][COD]BF_4$:

MS(ESI/pos. in CH_2Cl_2): m/z = 845 $[M^+-BF_4-COD-2H]$.